Korean Journal of Anesthesiology

Clinical Research Article

Korean J Anesthesiol 2025;78(3):261-271
https://doi.org/10.4097/kja.24540
pISSN 2005-6419 • eISSN 2005-7563

Received: August 5, 2024
Revised: October 2, 2024 (1st); November 27, 2024 (2nd)
Accepted: December 17, 2024

Corresponding author:
Gyu-Sam Hwang, M.D., Ph.D.
Department of Anesthesiology and Pain Medicine, Laboratory for Cardiovascular Dynamics, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea
Tel: +82-2-3010-3868
Fax: +82-2-470-1363
Email: kshwang@amc.seoul.kr
ORCID: https://orcid.org/0000-0002-3627-1107

© The Korean Society of Anesthesiologists, 2025
This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Liver transplantation outcomes in patients with primary tricuspid regurgitation with coaptation defects: a retrospective analysis in a high-volume transplant center

Kyoung-Sun Kim, Sun-Young Ha, Seong-Mi Yang, Hye-Mee Kwon, Sung-Hoon Kim, In-Gu Jun, Jun-Gol Song, Gyu-Sam Hwang

Department of Anesthesiology and Pain Medicine, Laboratory for Cardiovascular Dynamics, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Background: Cardiovascular diseases are the leading cause of mortality after liver transplantation (LT). Although the impact of secondary tricuspid regurgitation (TR) with severe pulmonary hypertension (PH) is well investigated, the impact of primary TR with tricuspid valve incompetence (TVI) on LT outcomes remains unclear. We aimed to investigate the prevalence and impact of primary TR with TVI on LT outcomes in a large-volume LT center.

Methods: We retrospectively examined 5512 consecutive LT recipients who underwent routine pretransplant echocardiography between 2008 and 2020. Patients were categorized based on the presence of anatomical TVI, specifically defined by incomplete coaptation, coaptation failure, prolapse, and flail leaflets of tricuspid valve (TV). Propensity score (PS)-based inverse probability weighting (IPW) was used to balance clinical and cardiovascular risk variables. The outcomes were one-year cumulative all-cause mortality and 30-day major adverse cardiovascular events (MACE).

Results: Anatomical TVI was identified in 14 patients (0.3%). Although rare, these patients exhibited significantly lower post-LT one-year survival rates (64.3% vs. 91.5%, $P < 0.001$) and higher 30-day MACE rates (42.9% vs. 16.9%, $P = 0.026$) than patients without TVI. They also had worse survival irrespective of echocardiographic evidence of PH ($P < 0.001$) and exhibited higher one-year mortality (IPW-adjusted hazard ratio: 4.09, $P = 0.002$) and increased 30-day MACE rates (IPW-adjusted odds ratio: 1.24, $P = 0.048$).

Conclusions: Primary TR with anatomical TVI was associated with significantly reduced one-year survival and increased post-LT MACE rates. These patients should be prioritized similarly to those with secondary TR with severe PH, with appropriate pretransplant evaluations and treatments to improve survival outcomes.

Keywords: Cardiovascular diseases; Echocardiography; Liver transplantation; Major adverse cardiac events; Mortality; Tricuspid regurgitation; Tricuspid valve insufficiency.

Introduction

The risk of cardiovascular diseases in patients with end-stage liver disease undergoing liver transplantation (LT) has recently gained attention. Cardiovascular complications have now surpassed graft rejection and infections as the leading cause of post-LT mortality [1]. Consequently, precise cardiac risk evaluation before LT is crucial for improving survival outcomes in these patients [2–4].

Tricuspid regurgitation (TR) is a relatively common valvular heart disease classified as either primary or secondary [5]. Typically, secondary TR is the most prevalent form and occurs due to higher pulmonary vascular resistance (PVR), enlargement of the right ventricle (RV) and/or right atrium (RA), and left-sided cardiac disease, causing increased pressure in the left atrium (LA) and left ventricle (LV). In contrast, primary TR, or anatomical TR, is caused by abnormalities in the tricuspid valve (TV) apparatus caused by congenital or acquired factors [6].

Among patients requiring LT, secondary or functional TR has been extensively investigated, primarily because of the high post-LT mortality associated with portopulmonary hypertension [7]. Nevertheless, there exists a considerable research gap regarding the adverse effects of anatomical TR, caused by TV coaptation abnormalities, prolapse, and flail, on transplant outcomes in a large cohort.

In this study, we aimed to investigate the effects of anatomical TV incompetence on major adverse cardiovascular events (MACE) and the one-year mortality rate after LT at a high-volume LT center. To mitigate potential biases arising from differences in patient demographics, we employed the inverse probability weighting (IPW) method using propensity score (PS) analysis.

Specifically, we examined whether anatomical TV incompetence, even in the absence of pulmonary artery hypertension (PAH), defined as peak TR velocity ≤ 2.8 m/s on echocardiography, was associated with worse post-LT outcomes compared with patients showing echocardiographic signs of PAH (peak TR velocity > 2.8 m/s).

Materials and Methods

Study population

All LT candidates were prospectively registered, and post-transplant outcomes were reviewed retrospectively. This analysis utilized data from our LT Registry between January 2008 and December 2020 to examine patients with anatomical TR.

Among 6482 patients, we enrolled 5815 consecutive LT candidates who underwent routine pre-LT echocardiography. A total of 303 patients were excluded, including 293 patients aged < 18 years and 10 patients with a history of cardiac valve surgery. Ultimately, 5512 patients who underwent echocardiographic evaluation of the TV were included in the analysis, with peak TR velocity measurements available for 3861 patients (Fig. 1).

The study design and a waiver of informed consent from participants were approved by the Institutional Review Board of Asan Medical Center, Seoul, Republic of Korea (protocol number 2023-0460).

Data collection

Baseline demographic, laboratory, echocardiographic, and perioperative data were collected from the fully computerized database of the institution. All laboratory variables were measured preoperatively and updated at the time of LT for repeated measurements. Standard preoperative two-dimensional transthoracic echocardiogram with Doppler and tissue Doppler imaging was performed within six months before LT, in accordance with the guidelines of the American Society of Echocardiography [8].

Evaluation of TV abnormalities

We retrieved information on TV abnormalities from the comments section of the formal transthoracic echocardiography reports. The 'grep' function in the R language was used to identify all instances of specific terms in the comprehensive echocardiogram report. Anatomical TV incompetence was specifically defined by incomplete coaptation, coaptation failure, prolapse, and flail leaflets of the TV. Mild TV incompetence was characterized by thickening, billowing, redundancy, and tethering of TV leaflets. This differentiation was made because mild TV incompetence is nonspecific and commonly observed in secondary TR associated with PAH.

Categorization of patients

Patients were categorized into two primary groups: those with anatomical TV incompetence (n = 14) and those without (n = 5498). They were further classified into three subgroups: no TV abnormality (n = 5433), mild TV incompetence (n = 65), and anatomical TV incompetence (n = 14). In the subgroup analysis, the 3,861 patients with peak TR velocity measurements were divided into three groups to assess the effects of anatomical TV incompetence, considering the coexistence of PAH. The three groups were as follows: patients with anatomical TV incompetence but no echocardiographic evidence of PAH (peak TR velocity ≤ 2.8 m/s, n = 8), patients without anatomical TV incompetence but with echocardiographic evidence of PAH (peak TR velocity > 2.8 m/s, n = 300), and patients with no echocardiographic evidence of PAH (n = 3553).

Outcomes and follow-up

Patient follow-up began on the day of LT surgery, and censored

https://doi.org/10.4097/kja.24540

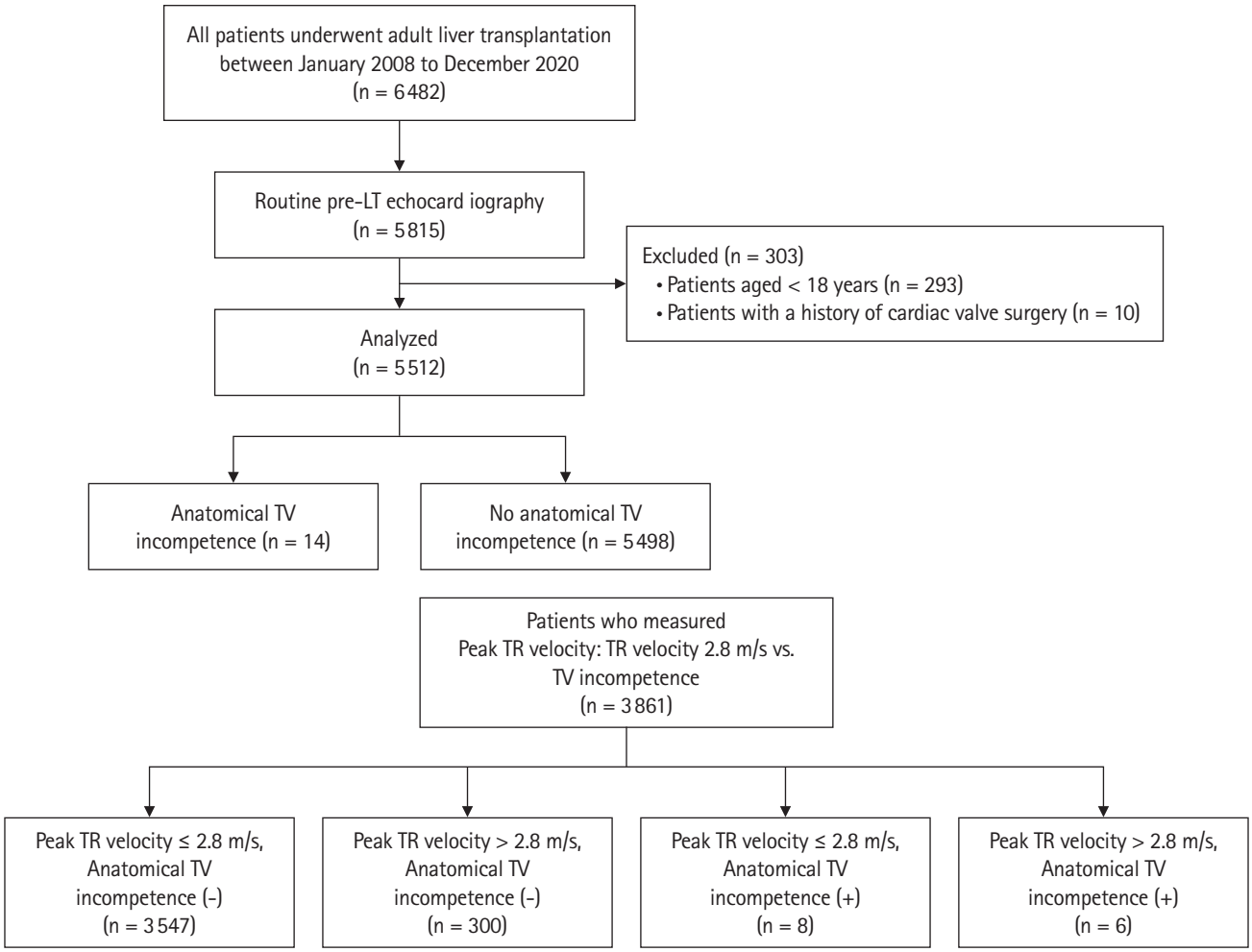


Fig. 1. Flowchart of study population and categorization.

data were followed up until December 2021. By December 2020, all patients had been followed up for at least one year post-LT, allowing for precise evaluation of the one-year mortality rate. Mortality data were regularly verified through our Organ Transplantation Center and information obtained from the Korean National Health Insurance System. Prior to analyzing the outcomes, one of the authors reconfirmed the mortality data. The primary outcome was the cumulative all-cause mortality at 365 days after LT. The secondary outcome was the 30-day MACE, defined as a composite of post-LT cardiovascular mortality, atrial fibrillation, ventricular arrhythmia, ST-T segment changes with chest tightness, myocardial infarction, pulmonary edema, pulmonary embolism, and stroke within 30 days post-LT.

Statistical analysis

Data are expressed as numbers with proportions for categorical variables and as medians with interquartile ranges (Q1, Q3) or means with standard deviation (SD) for continuous variables. Differences in continuous variables between groups were analyzed using the t-test or Mann–Whitney rank sum *U* test, while categorical variables were compared using the chi-square or Fisher's exact test as appropriate. Survival and MACE were compared using Kaplan–Meier survival functions with log-rank tests, multivariate logistic analysis, and Cox proportional hazards models to estimate adjusted hazard ratio (HR) or odds ratio (OR).

The IPW analysis based on PS was used to determine the differences in clinical and demographic characteristics between patients with and without anatomical TV incompetence. An average treatment effect on the treated (ATT) model that reweights the control group (those without anatomical TV incompetence) was used to match the treatment group (those with anatomical TV incompetence). The WeightIt package in R statistical software was utilized, enabling covariate balancing and stabilizing functions to generate balancing weights. Seven variables were incorporated to generate PS, including sodium adjusted model for

end-stage liver disease (MELD_Na) score > 20, age > 65 years, sex, body mass index (BMI), diabetes, hypertension, and the Revised Cardiac Risk Index (RCRI) ≥ 3. The RCRI was used to reduce the number of variables in the IPW analysis that is a widely validated model for evaluating cardiac risk during the perioperative period, including a history of ischemic heart disease, congestive heart failure, cerebrovascular disease, high-risk surgery (LT), preoperative insulin use, and preoperative creatinine level > 2 mg/dl (with each factor assigned a score of 1 point) [9]. The post-weighting balance in covariates was evaluated using standardized mean differences (SMDs), with SMDs > 0.1 indicating imbalance [10]. A love plot was generated to visually compare SMDs before and after weighting in PS analysis. An IPW-adjusted multivariable logistic and Cox regression analysis were performed to estimate the IPW-adjusted OR for MACE and HR for one-year post-LT mortality.

All statistical analyses were conducted using R, a language and environment for statistical computing (R core Team, 2024). The WeightIt package (Noah Greifer, 2024) was used for weighting procedures. R software (version 4.3.2) and the WeightIt package (1.3.2) are freely available at http://www.R-project.org.

Results

Clinical characteristics of the study population

The median age of the 5 512 patients was 54 years (48, 60, range: 18–79 years), and 72.6% of them were men. The primary causes of liver disease were hepatitis B or C virus-related liver diseases (61.6%), alcoholic liver diseases (23%), and other causes (17.8%). The prevalence rates of MELD_Na score > 20, age > 65 years, diabetes, hypertension, and RCRI ≥ 3 were 39.5%, 9.7%, 25.4%, 18.5%, and 7.1%, respectively. The median MELD_Na score was 15 (10, 24.5), and most LT surgeries were living-donor LT (82.7%). Table 1 summarizes the baseline demographic, laboratory, perioperative, and echocardiographic data of the patients (n = 5 512).

Prevalence and clinical characteristics of patients with anatomical TV incompetence

Fig. 2 illustrates a typical echocardiographic appearance of anatomical TV incompetence. Anatomical TV incompetence was detected in 14 patients (0.3%), comprising four incomplete coaptations, four coaptation failures, and six prolapses. No cases of TV leaflets flail were identified. However, 65 patients (1.2%) exhibited mild TV incompetence, including nine cases of thickening, two cases of billowing, 47 cases of tethering, and seven cases of leaflet redundancies.

Compared with patients without anatomical TV incompetence, those with anatomical TV incompetence had higher median MELD_Na score (25 vs. 15, P = 0.008), peak TR velocity (2.8 vs. 2.4 m/s, P < 0.001), and B-type natriuretic peptide (BNP) level (366.5 vs. 51 pg/L, P < 0.001). They also had a higher prevalence of pre-LT atrial fibrillation (14.3% vs. 1.7%, P = 0.010). However, age, sex, creatinine level, left ventricular ejection fraction, and the prevalence of diabetes, hypertension, and coronary artery disease were comparable between the two groups (Table 1).

Impact of anatomical TV incompetence on transplant outcomes

Of the patients who underwent LT (n = 5 512), 935 (16.9%) experienced MACE within 30 d, and 471 (8.5%) died within one year (Table 1). The Kaplan–Meier survival curve (Fig. 3A) showed that patients with anatomical TV incompetence had a significantly lower one-year survival rate of 64.3% (95% CI [43.5–95]) than those without anatomical TV incompetence (91.5%, 95% CI [90.8–92.3], P < 0.001). Patients with anatomical TV incompetence also had a higher MACE rate than those without anatomical TV incompetence (42.9% vs. 16.9%, P = 0.026; Table 1).

Among the three subgroups of patients (no TV abnormality [n = 5 433], mild TV incompetence [n = 65], and anatomical TV incompetence [n = 14]), patients with anatomical TV incompetence had significantly lower survival rates than those with mild TV incompetence and those without abnormalities (64.3% vs. 89.2% vs. 91.6%, Fig. 3B, P < 0.001). The Cox proportional hazards model showed that patients with anatomical TV incompetence had an unadjusted HR of 5.1 (95% CI [2.1–12.3], P < 0.001) and an adjusted HR of 4.09 (95% CI [1.69–9.88], P = 0.002) for one-year mortality. Regarding 30-day MACE, the unadjusted OR was 1.30 (95% CI [1.06–1.58], P = 0.010), and the adjusted HR was 1.23 (95% CI [1.02–1.50], P = 0.031) (Table 2).

Propensity-weighted comparison of transplant outcomes

Seven covariates were selected for the IPW analyses (MELD_Na score > 20, age > 65 years, sex, BMI, diabetes, hypertension, and RCRI ≥ 3). All variables demonstrated post-weighting balance with SMDs < 0.1 in a Love plot (Fig. 4).

Propensity-weighted analysis showed that patients with anatomical TV incompetence had an IPW-adjusted HR of 4.09 (95% CI [1.68–9.95], P = 0.002) for one-year mortality and an IPW-ad-

https://doi.org/10.4097/kja.24540

Table 1. Patient Demographics, Laboratory, Perioperative, and Echocardiographic Variables according to the Presence of Anatomical TVI

Variable	TVI absence (n = 5498)	TVI presence (n = 14)	Total (n = 5512)	P value
Demographic data				
Age (yr)	54 (48.0, 60.0)	60.0 (48.0, 63.0)	54.0 (48.0, 60.0)	0.187
Age > 65	530 (9.6)	2 (14.3)	532 (9.7)	0.893
Sex (M)	3992 (72.6)	10 (71.4)	4002 (72.6)	0.688
Viral-related liver disease	3385 (61.6)	10 (71.4)	3395 (61.6)	0.629
Alcoholic liver disease	1263 (23)	3 (21.4)	1266 (23)	1.000
Other disease	981 (17.8)	2 (14.3)	983 (17.8)	1.000
MELD_Na	15.0 (10.0, 24.5)	25.0 (15.0, 38.0)	15.0 (10.0, 24.5)	0.008
MELD_Na > 20	2167 (39.4)	9 (64.3)	2176 (39.5)	0.104
BMI (kg/m^2)	24 (21.7, 26.3)	23.2 (21.4, 26.6)	24 (21.7, 26.3)	0.973
Diabetes	1398 (25.4)	3 (21.4)	1401 (25.4)	0.971
Hypertension	1015 (18.5)	4 (28.6)	1019 (18.5)	0.530
Atrial fibrillation	94 (1.7)	2 (14.3)	96 (1.8)	0.010
Coronary artery disease	402 (7.3)	1 (7.1)	403 (7.3)	1.000
RCRI ≥ 3	388 (7.1)	2 (14.3)	390 (7.1)	0.160
Laboratory data				
Total bilirubin (mg/ml)	2.2 (1.1, 10.0)	8.4 (2.6, 25.3)	2.2 (1.1, 10.1)	0.018
Creatinine (mg/dl)	0.8 (0.7, 1.1)	1.0 (0.8, 1.6)	0.8 (0.7, 1.1)	0.098
BNP (pg/L)	55.0 (24.0, 131.0)	366.5 (125.0, 812.0)	55.0 (24.0, 132.0)	< 0.001
Donor and intraoperative variables				
Living donor (vs. deceased donor)	4550 (82.8)	7 (50)	4557 (82.7)	0.004
Massive transfusion*	2262 (41.1)	12 (85.7)	2274 (41.3)	0.002
Retransplantation	241 (4.4)	0 (0)	241 (4.4)	0.883
Preoperative transthoracic echocardiographic variables				
LV ejection fraction (%)	64.7 (61.6, 67.4)	64.9 (58.1, 68.3)	64.7 (61.6, 67.4)	0.715
End-systolic volume (ml)	38.0 (30.0, 46.0)	40.5 (28.0, 52.0)	38.0 (30.0, 46.0)	0.484
End-diastolic volume (ml)	106.0 (88.0, 129.0)	117.0 (83.0, 148.0)	106.0 (88.0, 129.0)	0.349
Mitral valve E/E'	9.0 (8.0, 11.0)	9.5 (7.0, 16.0)	9.0 (8.0, 11.0)	0.485
Peak TR (m/s)	2.4 (2.2, 2.6)	2.8 (2.6, 3.0)	2.4 (2.2, 2.6)	< 0.001
Posttransplant outcomes				
Thirty-day MACE	929 (16.9)	6 (42.9)	935 (17.0)	0.026
One-year mortality	466 (8.5)	5 (35.7)	471 (8.5)	0.002

Values are presented as median (Q1, Q3) or numer (%). *Massive transfusion was defined as the transfusion of ≥ 10 units of packed red blood cells. TVI: tricuspid valve incompetence, MELD_Na: sodium adjusted model for end-stage liver disease score, BMI: body mass index, RCRI: Revised Cardiac Risk Index, BNP: B-type natriuretic peptide, LV: left ventricle, E/E': ratio of transmitral Doppler early filling velocity to tissue Doppler early diastolic mitral annular velocity, TR: tricuspid regurgitation, MACE: major adverse cardiovascular events.

justed OR of 1.24 (95% CI [1.00–1.53], P = 0.048) for 30-day MACE (Table 2).

Subgroup analysis: impacts of anatomical TV incompetence, considering the coexistence of PH

Patients with anatomical TV incompetence but no echocardiographic signs of PAH had a significantly lower one-year survival rate of 50.0% (n = 8, 95% CI [25–100], P < 0.001) than those without anatomical TV incompetence but with echocardiographic evidence of PAH (n = 300, 84%, 95% CI [80–88.3]) — and a third group comprising the rest (n = 3553, 92.2%, 95% CI [91.4–93.1]). This indicates that anatomical TV incompetence had the worst post-transplant outcome, irrespective of the presence of PH (Fig. 5).

Discussion

Despite its rarity, this study is the first to show that LT recipients with anatomical TV incompetence experienced poorer transplant

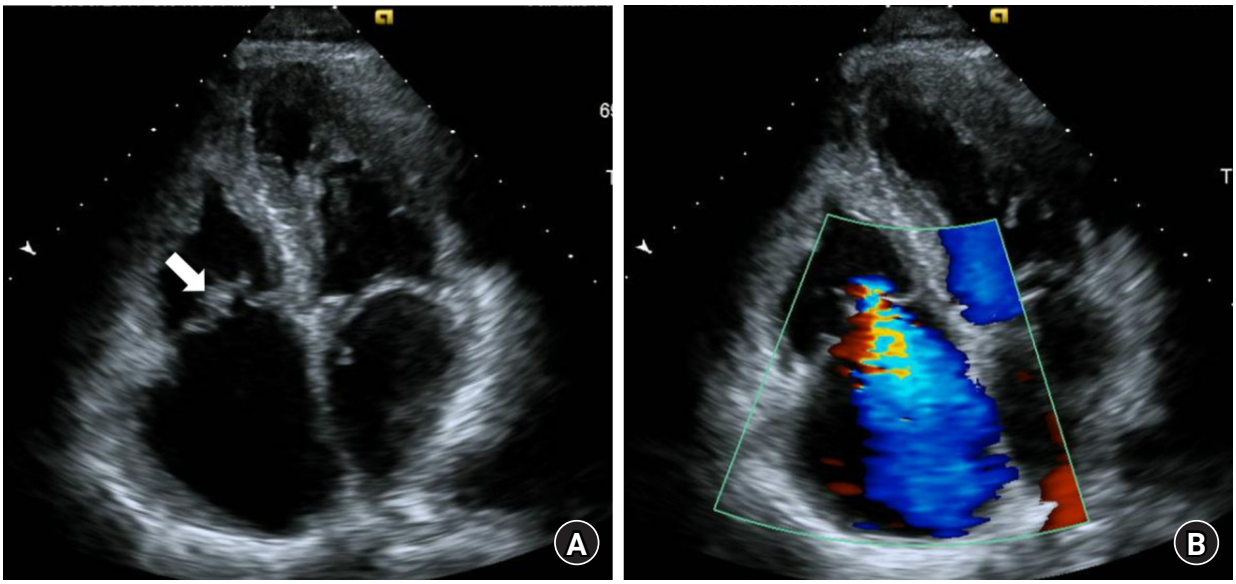


Fig. 2. (A) Pretransplant echocardiographic appearance of TVI, and (B) severe TR with color Doppler in a 37-year-old woman. The arrow indicates tricuspid valve coaptation failure during a systole. TVI: tricuspid valve incompetence, TR: tricuspid regurgitation.

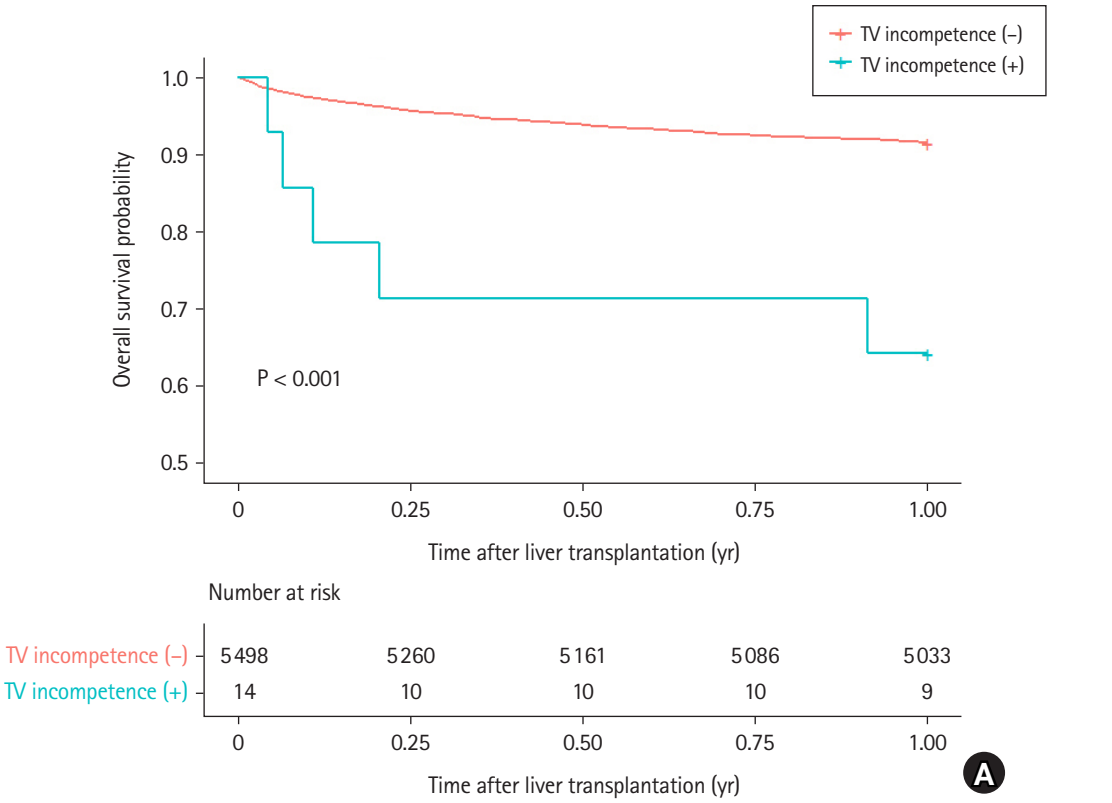
outcomes. These findings are remarkable as they are consistent with the well-known detrimental effects observed in patients with secondary TR and PH, even in cases of primary TR [11]. Patients with coaptation defects and prolapse in the TV exhibited significantly lower one-year survival rates than those without this valvular abnormality (64.3% vs. 91.5%, P < 0.001). In addition, the prevalence of MACE within 30 d after LT increased among patients with anatomical TV incompetence than in patients without this abnormality (42.9% vs. 16.9%, P = 0.026). Furthermore, these findings were consistent after conducting a propensity-weighted comparison of transplant outcomes, balancing covariates such as liver disease severity, age, sex, BMI, diabetes, hypertension, and RCRI parameters, including a history of ischemic heart disease, congestive heart failure, cerebrovascular disease, preoperative insulin use, and preoperative creatinine level. This analysis revealed an IPW-adjusted HR of 4.1 for one-year mortality (P = 0.002) and an IPW-adjusted OR of 1.24 for the 30-day MACE (P = 0.048). Moreover, the subgroup analysis indicated that even patients with anatomical TV incompetence but without echocardiographic signs of PAH had a significantly lower one-year survival rate. This finding highlights that anatomical TV incompetence had worse survival outcomes irrespective of the presence of PH.

Currently, there is a remarkable research gap concerning the impact of anatomical or primary TV incompetence that encompasses TV coaptation defects, prolapse, and flail on transplant outcomes in a comprehensive cohort. Most studies on TV dysfunction focused on secondary TR that results from the association between severe TR and PH in LT recipients. Therefore, this study is the first to systemically analyze the relationship between primary TR and post-LT outcomes.

TR is the most common lesion of the TV. Generally, trivial or mild TR is considered normal when the TV is structurally intact, affecting 65%–85% of the population [12,13]. However, moderate or severe TR, often associated with leaflet defects, annular dilation, or abnormalities in the papillary muscle, is typically pathological. Morphologically, primary or anatomical TR develops from inherent TV defects, either congenital or acquired. In contrast, secondary or functional TR results from changes in the TV caused by increased pressure or volume on the right or left side of the heart and pulmonary artery. Nonetheless, distinguishing primary and secondary TR can be challenging. Therefore, in this study, we specifically focused on severe anatomical TV incompetence, such as coaptation defects, prolapse, and flail, while excluding nonspecific abnormalities such as leaflet thickening, billowing, redundancy, and tethering. As anticipated, patients with severe anatomical TV incompetence had higher mortality rates than those with mild TV competence (P < 0.001, Fig. 3B).

The reciprocal impact of the heart and liver has long been recognized in clinical settings. Liver-related heart disease, such as cirrhotic cardiomyopathy, reveals how liver diseases affect the heart [14]. Conversely, congestive hepatopathy, also known as chronic passive hepatic congestion, occurs when the liver tissue becomes congested due to impaired outflow from the hepatic veins, typically caused by right-sided heart failure. Previous studies have reported that severe TR correlates with elevated choles-

https://doi.org/10.4097/kja.24540



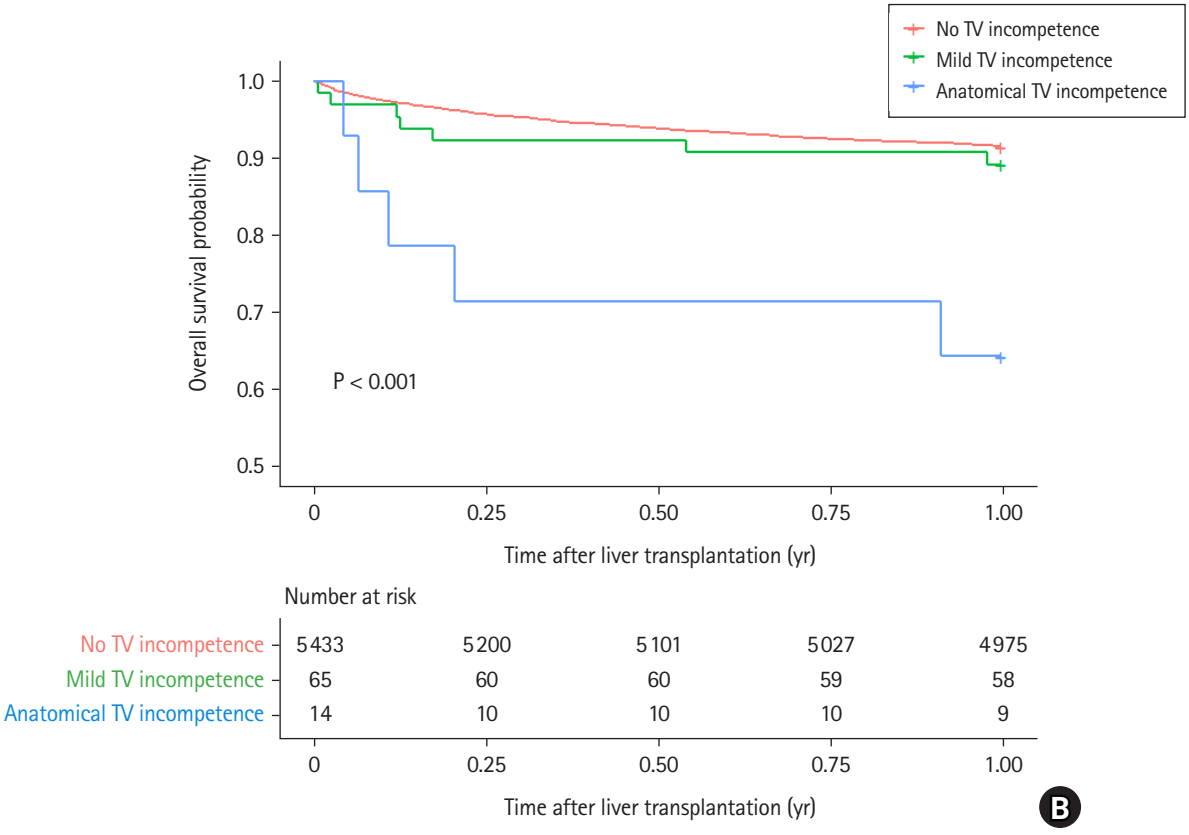


Fig. 3. Kaplan–Meier survival curves based on (A) the presence of anatomical TV incompetence (n = 14) and (B) three groups: no TV abnormality (n = 5433), mild TV incompetence (n = 65), and anatomical TV incompetence (n = 14). TV: tricuspid valve.

Table 2. Multivariable Cox and Logistic Regression Analysis and PS-Adjusted Analysis for One-Year Overall Mortality and 30-day MACE

Variable	One-year overall mortality					
	Univariate HR (95% CI)	P value	Multivariate adjusted HR (95% CI)	P value	IPW-adjusted HR	P value
TV incompetence	5.10 (2.11–12.32)	< 0.001	4.09 (1.69–9.88)	0.002	4.09 (1.68–9.95)	0.002
Age > 65 yr	2.03 (1.60–2.57)	< 0.001	2.00 (1.57–2.54)	< 0.001		
Sex (M)	0.87 (0.72–1.06)	0.177				
MELD_Na > 20	4.02 (3.29–4.90)	< 0.001	2.68 (2.14–3.34)	< 0.001		
BMI	0.94 (0.92–0.96)	< 0.001	0.95 (0.93–0.98)	< 0.001		
Diabetes	1.30 (1.07–1.59)	0.008				
Hypertension	1.07 (0.85–1.34)	0.579				
RCRI ≥ 3	1.88 (1.66–2.12)	< 0.001	1.43 (1.25–1.62)	< 0.001		
Variable	Thirty-day MACE					
	OR (95% CI)	P value	Multivariable adjusted OR (95% CI)	P value	IPW-adjusted OR	P value
TV incompetence	1.30 (1.06–1.58)	0.01	1.23 (1.02–1.50)	0.031	1.24 (1.00–1.53)	0.048
Age > 65 yr	1.17 (1.13–1.21)	< 0.001	1.16 (1.13–1.20)	< 0.001		
Sex (M)	0.99 (0.97–1.02)	0.637				
MELD_Na > 20	1.13 (1.11–1.15)	< 0.001	1.11 (1.09–1.13)	< 0.001		
BMI	1.00 (1.00–1.00)	0.586				
Diabetes	1.04 (1.02–1.07)	< 0.001				
Hypertension	1.03 (1.00–1.05)	0.032				
RCRI > 3	1.08 (1.07–1.10)	< 0.001	1.05 (1.03–1.07)	< 0.001		

PS: propensity score, MACE: major adverse cardiovascular events, HR: hazard ratio, TV: tricuspid valve, BMI: body mass index, OR: odds ratio, IPW: inverse probability weighting based on PS, TVI: tricuspid valve incompetence, MELD_Na: sodium adjusted model for end-stage liver disease score, RCRI: revised cardiac risk index.

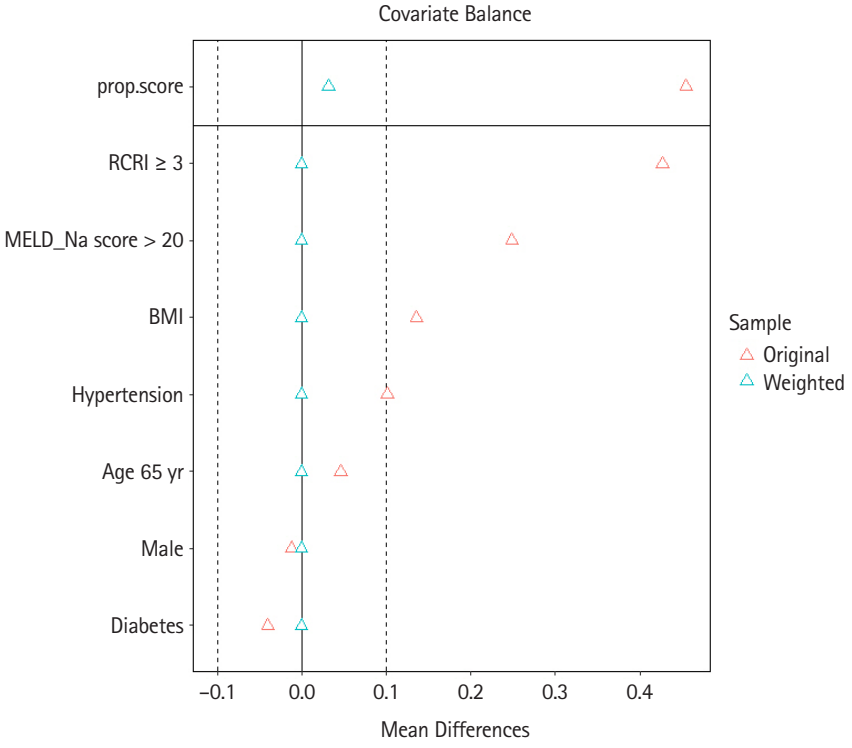


Fig. 4. Balance of seven covariates in a Love plot after IPW-based adjustment; all covariates showed SMDs < 0.1, indicating post-weighting balance. RCRI: revised cardiac risk index, MELD_Na: sodium adjusted model for end-stage liver disease score, BMI: body mass index, IPW: inverse probability weighting, SMD: standardized mean difference.

https://doi.org/10.4097/kja.24540

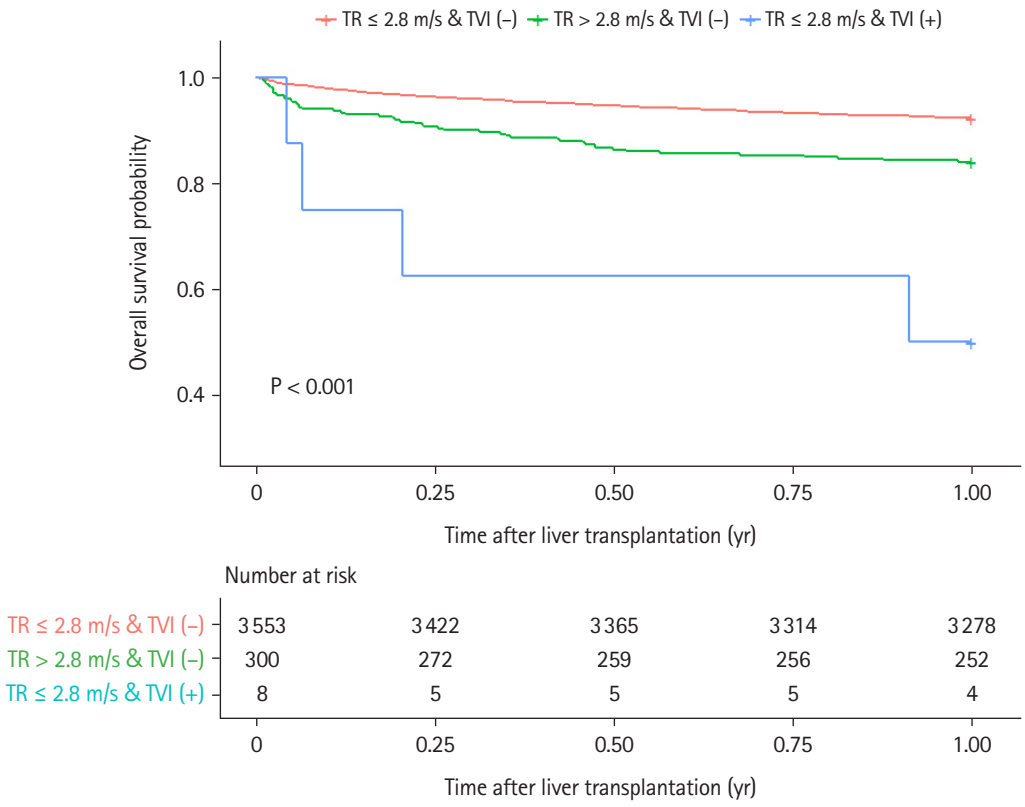


Fig. 5. Three groups based on anatomical TVI and presence of echocardiographic evidence of PH (TR > 2.8 m/s). The three groups are: TR ≤ 2.8 m/s & TVI (+), n = 8; TR > 2.8 m/s & TVI (-), n = 300; TR ≤ 2.8 m/s & TVI (-), n = 3553. TVI: tricuspid valve incompetence, TR: tricuspid regurgitation, PH: pulmonary hypertension.

tatic liver function tests and reduced albumin levels, suggesting that hepatic venule congestion and TR-induced pulsatile damage may contribute to liver dysfunction as much as, or more than, reduced cardiac output in heart failure. Histopathological studies have demonstrated central hepatic lobule hyperemia and congestion, with subsequent sinusoidal collagen deposition and septal fibrosis characteristic of nonischemic cardiac hepatopathy [15,16]. More importantly, anatomical TV incompetence can lead to progressive RA, RV, and annular dilatation, as well as conduction system abnormalities such as atrial fibrillation. These conditions may also be associated with reduced forward cardiac output and RV failure, with structural characteristics similar to those observed in secondary or functional TR [17]. In this study, patients with anatomical TV incompetence exhibited higher rates of preoperative atrial fibrillation (14.3% vs. 1.7%, P = 0.010) and higher BNP concentrations, indicating cardiac enlargement and elevated congestive load. These findings suggest that patients with anatomical TV incompetence may experience poorer survival and MACE outcomes after transplantation. Understanding the complex interactions between the heart and liver is increasingly crucial for optimizing treatment and improving the survival and prognosis of these patients [4].

Compared to mitral valve prolapse, TV prolapse is less recognized as a clinical entity, with its definition only recently proposed by Lorinsky et al. [18] in 2021 using echocardiography. They reported a 0.3% prevalence of suspected TV prolapse among 118442 individuals [19]. Normal atrial displacement of tricuspid leaflets can be up to 4 mm in the right ventricular inflow view and 2 mm in the four-chamber or parasternal short-axis view (PSAX). Using more than 2 mm in the PSAX view as a diagnostic criterion, 22% of patients with empirical TV prolapse had moderate-to-severe TR. However, the true prevalence of TV prolapse remains unclear [18,20]. In our cohort of 5512 patient, we observed a 0.3% prevalence of anatomical TV incompetence, including coaptation defects and TV prolapse. Guta et al. [20] found that patients with TV prolapse were more likely to have severe mitral regurgitation and advanced TR, independent of right ventricular systolic function.

Evaluating echocardiographic PH in severe TR poses significant challenges, despite echocardiography being a standard noninvasive method for evaluating TR severity. A recent study that compared invasive and echocardiographic methods for diagnos-

ing PH reported a sensitivity of 55% to echocardiography in adequately identifying patients with such cases. This underperformance may stem from Doppler echocardiography underestimating pulmonary arterial pressure in severe TR due to rapid pressure equalization between RA and RV, causing a loss of the pressure gradient between these chambers and results in underestimation of RA pressure in the presence of severe TR [21]. This mechanism could be applicable for patients with tricuspid incompetence in our study. Furthermore, subgroup analysis showed that even patients with anatomical TV incompetence but without echocardiographic signs of PAH exhibited significantly lower one-year survival rates, indicating that anatomical TV incompetence negatively impacts survival and PH.

Surgical intervention remains the preferred treatment for TR in patients presenting with acute right-sided heart failure [22]. Surgery can lower central venous pressure, halt RV remodeling, increase stroke volume, improve peripheral perfusion, and theoretically enable renal and hepatic recovery [23]. However, isolated TV surgery is considered a high-risk procedure due to high in-hospital mortality (10%), although markedly variable [24,25]. These risks are particularly pronounced in patients with nonvalvular left-sided heart disease by significantly elevated PVR and/or RV dysfunction that are associated with severe postprocedural outcomes [21]. Recently, transcatheter TV interventions have gained attention owing to their improved survival rates and reduced heart failure rehospitalization compared to medical therapy alone [23]. Furthermore, in LT recipients with anatomical TV incompetence, no research has explored the potential benefits of surgical or transcatheter TV before LT. Hence, further investigation into these therapeutic strategies is required.

Limitations

First, because this study was a retrospective observational analysis conducted at a single institution using electronic medical record data, a selection bias exists that may limit its generalizability. To mitigate this limitation, rigorous adjustments were applied using PS weighting analysis. Second, while the study analyzed over 5 000 patients with LT, anatomical TV incompetence was detected only in 14 patients (0.3%). This small sample size underscores the need for further investigation through an essentially larger, multicenter prospective design. Third, directly measured pulmonary arterial pressure data obtained from pulmonary arterial catheterization was not included in the analysis of pulmonary arterial hypertension effects. However, pulmonary artery catheterization is invasive, and current European Society of Cardiology guidelines recommend using peak TR velocity in echocardiography with a threshold of more than 2.8 m/s to diagnose high pulmonary arterial pressure.

In conclusion, although rare, our study showed that LT recipients with anatomical TV incompetence exhibited poorer transplant outcomes. This finding is significant because it mirrors the established poor survival rates of severe TR and PH in patients undergoing LT. Patients with anatomical TV incompetence should be prioritized for evaluation and management similar to those with severe PH. Integrating these findings into pretransplant cardiovascular assessments and implementing targeted treatment strategies could help improve survival outcomes in this population.

Acknowledgements

This research was partly supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: HR20C0026).

Funding

None.

Conflicts of Interest

Hye-Mee Kwon has been an editor for the Korean Journal of Anesthesiology since 2023. However, she was not involved in any process of review for this article, including peer reviewer selection, evaluation, or decision-making. There were no other potential conflicts of interest relevant to this article.

Data Availability

The datasets generated during and/or analyzed during the current study are not publicly available due to patient confidentiality and privacy protection but are available from the corresponding author on reasonable request.

Author Contributions

Kyoung-Sun Kim (Conceptualization; Data curation; Formal analysis; Methodology; Writing – original draft; Writing – review & editing)
Sun-Young Ha (Data curation; Investigation)
Seong-Mi Yang (Data curation; Formal analysis)
Hye-Mee Kwon (Data curation; Formal analysis; Investigation)
Sung-Hoon Kim (Methodology; Resources; Software)
In-Gu Jun (Data curation; Formal analysis)
Jun-Gol Song (Data curation; Methodology)
Gyu-Sam Hwang (Conceptualization; Methodology; Supervision; Writing – original draft; Writing – review & editing)

https://doi.org/10.4097/kja.24540

ORCID

Kyoung-Sun Kim, https://orcid.org/0000-0002-6643-9177
Sun-Young Ha, https://orcid.org/0009-0004-2920-3108
Seong-Mi Yang, https://orcid.org/0000-0002-4686-5822
Hye-Mee Kwon, https://orcid.org/0000-0001-7788-9555
Sung-Hoon Kim, https://orcid.org/0000-0001-5215-7585
In-Gu Jun, https://orcid.org/0000-0002-1225-1793
Jun-Gol Song, https://orcid.org/0000-0002-6076-6978
Gyu-Sam Hwang, https://orcid.org/0000-0002-3627-1107

References

1. VanWagner LB, Lapin B, Levitsky J, Wilkins JT, Abecassis MM, Skaro AI, et al. High early cardiovascular mortality after liver transplantation. Liver Transpl 2014; 20: 1306-16.
2. Kwon HM, Moon YJ, Kim KS, Shin WJ, Huh IY, Jun IG, et al. Prognostic value of B-type natriuretic peptide in liver transplant patients: implication in posttransplant mortality. Hepatology 2021; 74: 336-50.
3. Kwon HM, Moon YJ, Jung KW, Park YS, Kim KS, Jun IG, et al. Appraisal of cardiac ejection fraction with liver disease severity: implication in post-liver transplantation mortality. Hepatology 2020; 71: 1364-80.
4. Kwon HM, Hwang GS. Cardiovascular dysfunction and liver transplantation. Korean J Anesthesiol 2018; 71: 85-91.
5. Hahn RT, Lawlor MK, Davidson CJ, Badhwar V, Sannino A, Spitzer E, et al. Tricuspid valve academic research consortium definitions for tricuspid regurgitation and trial endpoints. Eur Heart J 2023; 44: 4508-32.
6. Hahn RT. Tricuspid regurgitation. N Engl J Med 2023; 388: 1876-91.
7. Krowka MJ, Miller DP, Barst RJ, Taichman D, Dweik RA, Badesch DB, et al. Portopulmonary hypertension: a report from the US-based REVEAL Registry. Chest 2012; 141: 906-15.
8. Mitchell C, Rahko PS, Blauwet LA, Canaday B, Finstuen JA, Foster MC, et al. Guidelines for performing a comprehensive transthoracic echocardiographic examination in adults: recommendations from the american society of echocardiography. J Am Soc Echocardiogr 2019; 32: 1-64.
9. Duceppe E, Parlow J, MacDonald P, Lyons K, McMullen M, Srinathan S, et al. Canadian cardiovascular society guidelines on perioperative cardiac risk assessment and management for patients who undergo noncardiac surgery. Can J Cardiol 2017; 33: 17-32.
10. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. Stat Med 2009; 28: 3083-107.
11. DuBrock HM. Portopulmonary hypertension: management and liver transplantation evaluation. Chest 2023; 164: 206-14.
12. Arsalan M, Walther T, Smith RL 2nd, Grayburn PA. Tricuspid regurgitation diagnosis and treatment. Eur Heart J 2017; 38: 634-8.
13. Singh JP, Evans JC, Levy D, Larson MG, Freed LA, Fuller DL, et al. Prevalence and clinical determinants of mitral, tricuspid, and aortic regurgitation (the Framingham Heart Study). Am J Cardiol 1999; 83: 897-902.
14. Barman PM, VanWagner LB. Cardiac risk assessment in liver transplant candidates: current controversies and future directions. Hepatology 2021; 73: 2564-76.
15. Lau GT, Tan HC, Kritharides L. Type of liver dysfunction in heart failure and its relation to the severity of tricuspid regurgitation. Am J Cardiol 2002; 90: 1405-9.
16. Simonetto DA, Yang HY, Yin M, de Assuncao TM, Kwon JH, Hilscher M, et al. Chronic passive venous congestion drives hepatic fibrogenesis via sinusoidal thrombosis and mechanical forces. Hepatology 2015; 61: 648-59.
17. Adler DS. Non-functional tricuspid valve disease. Ann Cardiothorac Surg 2017; 6: 204-13.
18. Lorinsky MK, Belanger MJ, Shen C, Markson LJ, Delling FN, Manning WJ, et al. Characteristics and significance of tricuspid valve prolapse in a large multidecade echocardiographic study. J Am Soc Echocardiogr 2021; 34: 30-7.
19. Han Y, Chen T, Addetia K. Tricuspid valve prolapse: a forgotten mechanism of primary tricuspid regurgitation? J Am Coll Cardiol 2023; 81: 894-6.
20. Guta AC, El-Tallawi KC, Nguyen DT, Qamar F, Nguyen T, Zoghbi WA, et al. Prevalence and clinical implications of tricuspid valve prolapse based on magnetic resonance diagnostic criteria. J Am Coll Cardiol 2023; 81: 882-93.
21. Lurz P, Orban M, Besler C, Braun D, Schlotter F, Noack T, et al. Clinical characteristics, diagnosis, and risk stratification of pulmonary hypertension in severe tricuspid regurgitation and implications for transcatheter tricuspid valve repair. Eur Heart J 2020; 41: 2785-95.
22. Chioncel O, Adamo M, Nikolaou M, Parissis J, Mebazaa A, Yilmaz MB, et al. Acute heart failure and valvular heart disease: a scientific statement of the Heart Failure Association, the Association for Acute CardioVascular Care and the European Association of Percutaneous Cardiovascular Interventions of the European Society of Cardiology. Eur J Heart Fail 2023; 25: 1025-48.
23. Taramasso M, Benfari G, van der Bijl P, Alessandrini H, Attinger-Toller A, Biasco L, et al. Transcatheter versus medical treatment of patients with symptomatic severe tricuspid regurgitation. J Am Coll Cardiol 2019; 74: 2998-3008.
24. Dreyfus J, Audureau E, Bohbot Y, Coisne A, Lavie-Badie Y, Bouchery M, et al. TRI-SCORE: a new risk score for in-hospital mortality prediction after isolated tricuspid valve surgery. Eur Heart J 2022; 43: 654-62.
25. Axtell AL, Bhambhani V, Moonsamy P, Healy EW, Picard MH, Sundt TM 3rd, et al. Surgery does not improve survival in patients with isolated severe tricuspid regurgitation. J Am Coll Cardiol 2019; 74: 715-25.